Remarks

Applicants acknowledge and thank the Examiner for careful consideration and allowance of claims 28-35. *See*, Paper No. 16, page 2, item 5. Applicants have herein canceled claims 44-47 without prejudice or disclaimer. Applicants have amended claims 21, 36-37, 43, 48-49, 55-56, and 59-60 to comply with the Examiner's suggestions (discussed below). Applicants have also cancelled claims 38-42 and re-presented these in independent form (claims 62-67) as suggested by the Examiner. *See*, Paper No. 16, page 2, item 6. Accordingly, the subject matter of claims 38-42 has been incorporated into independent Markush-type claim 62. Upon entry of the present amendment, claims 21-26, 28-37, 43, 48-49, 54-56, 58-60, and 62-67 will be pending. No new matter has been added.

I. Amendments to the Specification

Applicants have also discovered an obvious typographical error in the specification. Accordingly, the specification has been amended with respect to correction of the NaCl and trisodium citrate concentrations for 5xSSC disclosed on page 12, lines 28-29 of the specification. An amendment to correct an obvious error does not constitute new matter where one skilled in the art would not only recognize the existence of the error in the specification, but also the appropriate correction. *See*, M.P.E.P. § 2163.07. Here, the recognition of the typographical errors, along with the correction of the errors in the specification and claims and in the ingredient amounts listed for 5x SSC is obvious to one skilled in the art; therefore, the correction does not constitute new matter.

In particular, 5x SSC is a component of many hybridization solutions and is well known in the art. (*See*, e.g., Exhibit A, CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley and Sons, N.Y., at page 2.10.7 (1989)). SSC is normally made as a 20x stock solution, and then diluted accordingly for a particular use. Exhibit A also shows that a 20x SSC stock solution contains 3 M NaCl and 0.3 M trisodium citrate. (*See*, e.g., Exhibit A, CURRENT PROTOCOLS, at page A.2.5.) To make a 5x SSC solution, the 20x solution must be diluted by a factor of four. Therefore, a 5x SSC solution contains 750 mM NaCl (3 M ÷ 4 = 750 mM) and 75 mM trisodium citrate (0.3 M − 4 = 75 mM). One skilled in the art would have immediately recognized that the amounts of ingredients

listed in the specification for a 5x SSC solution was incorrect. Rather than describing a 5x SSC solution, made up of 750 mM NaCl and 75 mM trisodium citrate, the specification inaccurately listed the ingredient amounts for a 1x solution. The skilled artisan, in recognizing the typographical error, could have easily adjusted the amount of ingredients described in the specification to properly make a 5x SSC solution.

Therefore, because no new matter will be added to the specification if these typographical errors are corrected, Applicants respectfully request that the amendments to the specification to recite the correct concentrations of sodium chloride and sodium citrate in 5x SSC be entered.

II. Claims 38-42

Claims 38-42 were objected to as being dependent upon a rejected base claim, "but would be allowable if rewritten in independent form..." *See*, Paper No. 16, page 2, item 6.

Applicants have herein amended independent claim 36, upon which claims 38-42 depend, in order to comply with the Examiner's rejection of this claim (discussed further below). Upon allowance of claim 36, the objection to claims 38-42 will become moot. Accordingly, Applicants respectfully request that the objection to claims 38-42 be withdrawn upon allowance of claim 36.

III. 35 U.S.C. § 112, first paragraph

A. Claims 21-26, 36, 37, 43-49, 54-56 and 58-60 were rejected under 35 U.S.C. § 112, first paragraph. *See*, Paper No. 16 page 3, item 9 and, page 5, item 10. In particular the Examiner objected to the absence of "the population of neurons that this polypeptide putatively exerts any definable and assayable function recited in the claims..." *See*, Paper No. 16, page 4, first paragraph.

Accordingly, Applicants have herein amended independent claim 21 (and thereby dependent claims 22-26, 54, and 58) to recite "promotes axonal neurite extension" and to recite "dorsal spinal cord neurons". Support for this assay, on this population of neurons, can be found in the specification as filed, for example, at page 28, first and second paragraphs. Therefore, no new matter has been added by the amendment.

B. The Examiner also asserted that "'consisting of at least...' is no different from 'comprising' language..." *See*, Paper No. 16, page 6, first full paragraph.

Applicants disagree with the Examiner's characterization but have herein amended independent claims 36 and 43 (and thereby dependent claims 37, 48-49, 55-56, and 59-60) to remove "consisting of" and to include clarification that the claimed polypeptides are *fragments*. Additionally, Applicants have also amended claim 43 (and thereby dependent claims 48-49, 56, and 60) to include to include a definable assay and specific neuron population (*i.e.*, "promotes axonal neurite extension of dorsal spinal cord neurons").

Last, Applicants have herein canceled claim 44-47 thereby rendering rejection of these claims moot.

In view of the above explanations and amendments Applicants respectfully request that the rejections and objections to claims 21-26, 36, 37, 43-49, 54-56 and 58-60 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

Conclusion

Applicants believe that this application is in condition for allowance. The Examiner is invited to call the undersigned at the phone number provided below if any further action by Applicants would expedite the allowance of this application.

Applicants believe that there are no fees due in connection with the filing of this paper. However, should a fee be due, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136, such an extension is requested and the appropriate fee should also be charged to our Deposit Account.

Respectfully submitted,

Dated: July 1, 2003

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KKH/MJH/DAS
Enclosures

Exhibit A

CURRENT PROTOCOLS IN MOLECULAR BIOLOGY

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1c. *Harsh treatment:* Pour several hundred milliliters of boiling 0.1% SDS onto the membrane. Cool to room temperature.

If a membrane is to be reprobed, it must not be allowed to dry out between hybridization and stripping. If it becomes dry, the probe may bind to the matrix.

2. Place membrane on a sheet of dry Whatman 3MM filter paper and blot excess liquid with a second sheet. Wrap the membrane in plastic wrap and set up an autoradiograph.

If signal is still seen after autoradiography, rewash using harsher conditions.

3. The membrane can now be rehybridized. Alternatively, it can be dried and stored for later use.

Membranes can be stored dry between Whatman 3MM paper for several months at room temperature. For long-term storage, place the membranes in a desiccator at room temperature or 4°C.

REAGENTS AND SOLUTIONS

Aqueous prehybridization/hybridization (APH) solution

5× SSC (APPENDIX 2)
5× Denhardt solution (APPENDIX 2)
1% (w/v) SDS

Add 100 µg/ml denatured salmon sperm DNA (see below) just before use

Alternatives to Denhardt solution and denatured salmon sperm DNA as blocking agents are listed in Table 2.10.5 (see discussion in critical parameters).

Denatured salmon sperm DNA

Dissolve 10 mg Sigma type III salmon sperm DNA (sodium salt) in 1 ml water. Pass vigorously through a 17-G needle 20 times to shear the DNA. Place in a boiling water bath for 10 min, then chill. Use immediately or store at −20°C in small aliquots. If stored, reheat to 100°C for 5 min and chill on ice immediately before using.

Formamide prehybridization/hybridization (FPH) solution

5× SSC (APPENDIX 2)
5× Denhardt solution (APPENDIX 2)
50% (w/v) formamide
1% (w/v) SDS

Add 100 µg/ml denatured salmon sperm DNA (see above) just before use

Alternatives to Denhardt solution and denatured salmon sperm DNA as blocking agents are listed in Table 2.10.5 (see discussion in critical parameters).

Commercial formamide is usually satisfactory for use. If the liquid has a yellow color, deionize as follows: add 5 g of mixed-bed ion-exchange resin [e.g., Bio-Rad AG 501-X8 or 501-X8(D) resins] per 100 ml formamide, stir at room temperature for 1 hr, and filter through Whatman no. 1 paper.

CAUTION: *Formamide is a teratogen. Handle with care.*

Labeling buffer

200 mM Tris·Cl, pH 7.5
30 mM $MgCl_2$
10 mM spermidine

Mild stripping solution

5 mM Tris·Cl, pH 8.0
2 mM EDTA
0.1× Denhardt solution (APPENDIX 2)

SDS electrophoresis buffer, 5×

15.1 g Tris base
72.0 g glycine
5.0 g SDS
H_2O to 1000 ml
Dilute to 1× or 2× for working solution, as appropriate

Do not adjust the pH of the stock solution, as the solution is pH 8.3 when diluted. Store at 0° to 4°C until use (up to 1 month).

SED (standard enzyme diluent)

20 mM Tris-Cl, pH 7.5
500 µg/ml bovine serum albumin (Pentax Fraction V)
10 mM 2-mercaptoethanol
Store up to 1 month at 4°C

Sodium acetate, 3 M

Dissolve 408 g sodium acetate-$3H_2O$ in 800 ml H_2O
Add H_2O to 1 liter
Adjust pH to 4.8 or 5.2 (as desired) with 3 M acetic acid

Sodium acetate buffer, 0.1 M

Solution A: 11.55 ml glacial acetic acid/liter (0.2 M).
Solution B: 27.2 g sodium acetate ($NaC_2H_3O_2 \cdot 3H_2O$)/liter (0.2 M).

Referring to Table A.2.2 for desired pH, mix the indicated volumes of solutions A and B, then dilute with H_2O to 100 ml. (See Potassium acetate buffer recipe for further details.)

Sodium phosphate buffer, 0.1 M

Solution A: 27.6 g $NaH_2PO_4 \cdot H_2O$ per liter (0.2 M).
Solution B: 53.65 g $Na_2HPO_4 \cdot 7H_2O$ per liter (0.2 M).

Referring to Table A.2.3 for desired pH, mix the indicated volumes of solutions A and B, then dilute with H_2O to 200 ml. (See Potassium phosphate buffer recipe for further details.)

SSC (sodium chloride/sodium citrate), 20×

3 M NaCl (175 g/liter)
0.3 M Na_3citrate-$2H_2O$ (88 g/liter)
Adjust pH to 7.0 with 1 M HCl

STE buffer

10 mM Tris-Cl, pH 7.5
10 mM NaCl
1 mM EDTA, pH 8.0

TAE (Tris/acetate/EDTA) electrophoresis buffer

50× stock solution:	*Working solution, pH ~8.5:*
242 g Tris base	
57.1 ml glacial acetic acid	40 mM Tris-acetate
37.2 g $Na_2EDTA \cdot 2H_2O$	2 mM $Na_2EDTA \cdot 2H_2O$
H_2O to 1 liter	

TBE (Tris/borate/EDTA) electrophoresis buffer

10× stock solution, 1 liter:
108 g Tris base (890 mM)
55 g boric acid (890 mM)
40 ml 0.5 M EDTA, pH 8.0 (20 mM)